Complete Summary

GUIDELINE TITLE

Lipid modification. Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Primary Care. Lipid modification. Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 37 p. (Clinical guideline; no. 67).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- July 1, 2009 - Chantix or Champix (Varenicline) and Zyban or Wellbutrin (bupropion or amfebutamone): The U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that it has required the manufacturers of the smoking cessation aids varenicline (Chantix) and bupropion (Zyban and generics) to add new Boxed Warnings and develop patient Medication Guides highlighting the risk of serious neuropsychiatric symptoms in patients using these products. These symptoms include changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Cardiovascular disease (CVD)
- Dyslipidemia
- Hypercholesterolemia

GUIDELINE CATEGORY

Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Geriatrics
Internal Medicine
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Dietitians
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations about lifestyle modification, drug therapy, patient information and the communication of patient risk assessment and information surrounding lipid modification for primary and secondary prevention of cardiovascular disease (CVD)

TARGET POPULATION

Adults aged 18 and older who have established cardiovascular disease (CVD) (including coronary heart disease [CHD, angina only], stroke or peripheral arterial disease) or who are at high risk of developing CVD because of a combination of CVD risk factors including raised blood pressure and hypertension, overweight and obesity.

The following special groups have been considered for primary prevention: black and minority ethnic groups, in particular South Asians; people with a family history of CHD; low socioeconomic groups.

Note: The guideline does not cover:

- People with diabetes
- People with familial monogenic lipid disorders
- People at high risk of CVD as a result of secondary disease processes or drug treatment

Refer to the full version of the original guideline document (see the "Availability of Companion Documents" field) for detailed information on target population.

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Risk Assessment/Prevention

1. Assessment of cardiovascular risk including age, sex, ethnicity, blood pressure, body mass index, lipid measurements, fasting blood glucose, liver and renal function, smoking status, alcohol consumption, thyroid-stimulating hormone (TSH), family history of premature heart disease, and using the Framingham 1991 10-year risk equations
2. Communicating information about risk assessment and treatment
3. Primary prevention of cardiovascular disease (CVD)
    - Lifestyle modifications including cardioprotective diet, physical activity, weight management, smoking cessation, limiting alcohol consumption
    - Drug therapy including statins (simvastatin or pravastatin) and ezetimibe (for patients with primary hypercholesterolemia)

    Note: The following treatments were considered but not recommended for the primary prevention of CVD: routine taking of plant sterols and stanols, fibrates, nicotinic acid, anion exchange resins, and combination therapies of any of these drugs with a statin.

4. Secondary prevention of CVD:
    - Lifestyle modifications (diet, physical activity, weight management, etc.)
    - Drug therapy including statins (simvastatin or pravastatin), fibrates, nicotinic acid, anion exchange resins, and ezetimibe (for patients with primary hypercholesterolemia)
5. Monitoring of treatment

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness of primary and secondary prevention of cardiovascular disease (CVD)
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC):Â This guideline was developed by the National Collaborating Centre forÂ Primary Care on behalf of the National Institute for Health and Clinical Excellence (NICE). SeeÂ the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Effectiveness

Literature Search Strategy

The purpose of searching the literature is to identify published evidence that can be used to answer the clinical questions identified by the methodology team and the Guideline Development Group (GDG) (The total list of key clinical questions identified is shown in Appendix F of the full version of the original guideline document [seeÂ the "Availability of Companion Documents" field]). The Information Scientist developed search strategies for each searchable question, with guidance from the GDG, using relevant MeSH (medical subject headings) or indexing terms, and relevant free text terms. Searches were conducted between September 2005 and August 2006. The Information Specialist agreed in advance with the Reviewer and Health Economist the sources to be searched for a given question. The parameters of literature searches, including any population limits and exclusions, were detailed on pro formas developed for each question. Updated searches for each question, to identify recent evidence, were carried out in April 2007. Full details of the sources and databases searched and the search strategies are contained in Appendix F of the full version of the original guideline document (seeÂ the "Availability of Companion Documents" field).

An initial search for published guidelines or systematic reviews was carried out on the following databases or websites: National Electronic Library for Health (NeLH) Guidelines Finder, National Guidelines Clearinghouse, Scottish Intercollegiate Guidelines Network (SIGN), Guidelines International Network (GIN), Canadian Medical Association (CMA) Infobase (Canadian guidelines), National Health and Medical Research Council (NHMRC) Clinical Practice Guidelines (Australian Guidelines), New Zealand Guidelines Group, British Medical Journal (BMJ) Clinical Evidence, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and Heath Technology Assessment Database (HTA).

If a recent, high quality, systematic review or guideline was identified to answer a clinical question, then in some instances no further searching was carried out.

Depending on the question, some or all of the following bibliographic databases were also searched to the latest date available: MEDLINE, EMBASE, CINAHL, CENTRAL (Cochrane Controlled Trials Register), PsycINFO, Allied & Complementary Medicine (AMED).

Identifying the Evidence

After the search of titles and abstracts was undertaken, full papers were obtained if — based on abstract and title — they appeared relevant to the topic addressed in the GDG's question. The highest level of evidence was sought first. Wherever appropriate, the searches for evidence for both primary and secondary cardiovascular disease prevention were conducted simultaneously, and the results of these were then scanned to address separate questions.Â Where randomised controlled trials were not available, observational studies, surveys and expert formal consensus results were used. Only papers published in English were reviewed. Following a critical review of the full version of the study, articles not relevant to the subject in question were excluded. Studies that did not report on relevant outcomes were also excluded. Submitted evidence from stakeholders was included where the evidence was relevant to the GDG's clinical question and when it was either better or equivalent in quality to the research identified in the literature searches. Specialist advice was obtained from a dietitian to aid in the identification of useful terms for inclusion in searches for questions relating to lifestyle interventions.

The reasons for rejecting any paper ordered were recorded.

Cost-Effectiveness

Literature Review for Health Economics

The following information sources were searched: Medline (Ovid) (1966-April 2007), Embase (1980-April 2007), National Health Service Economic Evaluations Database (NHS EED), PsycINFO and Cumulative Index to Nursing and Allied Health Literature (CINAHL).

The electronic search strategies were developed in Medline and adapted for use with the other information databases. The clinical search strategy was supplemented with economic search terms. The Information Scientist carried out the searches for health economics evidence. Identified titles and abstracts from the economic searches were reviewed by a single health economist and full papers obtained as appropriate. No criteria for study design were imposed a priori. In this way the searches were not constrained to randomised controlled trials (RCTs) containing formal economic evaluations.

Papers were included if they were full/partial economic evaluations, considered patients at risk of or those who have had a cardiovascular event. Thus, patients who have had stroke, angina, peripheral artery disease, transient ischaemic stroke or myocardial infarction were considered for the secondary prevention section. Only papers written in English were considered.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Primary Care on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Effectiveness

Critical Appraisal of the Evidence

The Systematic Reviewer synthesised the evidence from the papers retrieved for each question or questions into a narrative summary. These formed the basis of this guideline. Each study was critically appraised using National Institute for Health and Clinical Excellence (NICE) criteria for quality assessment. The information extracted from the included studies is given in Appendices D and E of the full version of the original guideline document (see the "Availability of Companion Documents" field). Background papers, for example those used to set the clinical scene in the narrative summaries, were referenced but not extracted.

Cost-Effectiveness

The full papers were critically appraised by the health economist using a standard validated checklist. A general descriptive overview of the studies, their quality, and conclusions was presented and summarised in the form of a narrative review.

Cost-Effectiveness Modelling

Some areas were selected for further economic analysis if there was likelihood that the recommendation made would substantially change clinical practice in the National Health Service and have important consequences for resource use. For this guideline three areas were chosen for further economic analysis:

- Cost-effectiveness of strategies for identification of patients at high risk of cardiovascular disease (CVD) in primary care
- Cost-effectiveness of high intensity statins compared with lower intensity statins in patients with coronary heart disease
- Cost-effectiveness of a strategy of 'titration threshold' (treating to target of 5 mmol/l and 4 mmol/l) compared with a strategy of using a standard dose of statin in people with CVD including a full incremental analysis

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre forÂ Primary Care on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Key Clinical Questions

The first step in the development of the guideline was to refine the guideline scope into a series of key clinical questions (KCQs). The KCQs were developed by the Guideline Development Group (GDG) with assistance from the methodology team. The total list of KCQs identified is shown in Appendix F of the full version of the original guideline document (see the "Availability of Companion Documents" field).

Forming Recommendations

The GDG met at 4- to 5- week intervals for 18 months to review the evidence identified by the Development Team, to comment on its quality and relevance and to develop recommendations for clinical practice based on the available evidence.

In preparation for each meeting, the narrative and extractions for the questions being discussed were made available to the GDG one week before the scheduled GDG meeting. These documents were available on a closed intranet site and sent by post to those members who requested it.

GDG members were expected to have read the narratives and extractions before attending each meeting. The GDG discussed the evidence at the meeting and agreed evidence statements and recommendations. Any changes were made to the electronic version of the text on a laptop and projected onto a screen until the GDG were satisfied with them.

All work from the meetings was posted on the closed intranet site following the meeting as a matter of record and for referral by the GDG members.

The recommendations and evidence statements were posted on an electronic forum. The discussion was reviewed at the next meeting and the recommendations finalised.

Areas without Evidence and Consensus Methodology

The table of clinical questions in Appendix F of the full version of the guideline (see the "Availability of Companion Documents" field) indicates which questions were searched.

In cases where evidence was sparse, or where the question was not deemed searchable, the GDG derived the recommendations via informal consensus methods (for example in the case of Question 23: 'How necessary is it to monitor liver function tests?').

In a few cases where there was a lack of consensus, a formal vote was taken. Cooptees and GDG members with a declared interest did not vote.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost-Effectiveness Modelling

Some areas were selected for further economic analysis if there was likelihood that the recommendation made would substantially change clinical practice in the National Health Service (NHS) and have important consequences for resource use. For this guideline three areas were chosen for further economic analysis:

- Cost-effectiveness of strategies for identification of patients at high risk of cardiovascular disease (CVD) in primary care
- Cost-effectiveness of high intensity statins compared with lower intensity statins in patients with coronary heart disease
- Cost-effectiveness of a strategy of 'titration threshold' (treating to target of 5 mmol/l and 4 mmol/l) compared with a strategy of using a standard dose of statin in people with CVD including a full incremental analysis

Full reports for each topic are in Appendix C of the full version of the original guideline document (see the "Availability of Companion Documents" field). The Guideline Development Group (GDG) was consulted during the construction and interpretation of each model to ensure that appropriate assumptions, model structure and data sources were used.

All models were constructed in accordance with the National Institute for Health and Clinical Excellence (NICE) reference case outlined in the 'Guideline technical manual' (2007).

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations:

1. The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with

Stakeholders and comments were considered by the Guideline Development Group (GDG).
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre forÂ Primary Care on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Identification and Assessment of Cardiovascular Disease (CVD) Risk

Identifying People for Full Formal Risk Assessment

For the primary prevention of CVD in primary care, a systematic strategy should be used to identify people aged 40 to 74 who are likely to be at high risk.

People should be prioritised on the basis of an estimate of their CVD risk before a full formal risk assessment. Their CVD risk should be estimated using CVD risk factors already recorded in primary care electronic medical records.

People older than 40 should have their estimate of CVD risk reviewed on an ongoing basis.

People should be prioritised for a full formal risk assessment if their estimated 10-year risk of CVD is 20% or more.

Healthcare professionals should discuss the process of risk assessment with the person identified as being at risk, including the option of declining any formal risk assessment.

Opportunistic assessment should not be the main strategy used in primary care to identify CVD risk in unselected people.

Full Formal Risk Assessment

Healthcare professionals should always be aware that all CVD risk estimation tools can provide only an approximation of CVD risk. Interpretation of CVD risk scores should always reflect informed clinical judgement.

The Framingham 1991 10-year risk equations should be used to assess CVD risk. CVD risk should be calculated as:

CVD risk = 10-year risk of fatal and non-fatal stroke, including transient ischaemic attack + 10-year risk of coronary heart disease (CHD)

Note: CHD risk includes the risks of death from CHD, and non-fatal CHD, including silent myocardial infarction, angina, and coronary insufficiency (acute coronary syndrome).

The following variables should be used for formal estimation of CVD risk with the Framingham 1991 equations:

- Age
- Sex
- Systolic blood pressure (mean of previous two systolic readings)
- Total cholesterol
- High density lipoprotein (HDL) cholesterol
- Smoking status
- Presence of left ventricular hypertrophy

The Framingham 1991 risk equations should not be used for people with pre-existing:

- CHD or angina
- Stroke or transient ischaemic attack
- Peripheral vascular disease

The Framingham risk equation should not be used for people who are already considered at high risk of CVD because of:

- Familial hypercholesterolaemia or other monogenic disorders of lipid metabolism
- Diabetes, see 'Type 2 diabetes: the management of type 2 diabetes (update)' (NICE clinical guideline 66).

Healthcare professionals should be aware that Framingham 1991 risk equations may overestimate risk in UK populations.

When using the risk score to inform drug treatment decisions, particularly if it is near to the threshold of 20%*, healthcare professionals should consider other factors that:

- May predispose the person to premature CVD
- May not be included in calculated risk scores

*This threshold is from the National Guideline Clearinghouse (NGC) summary of the National Institute of Health and Clinical Excellence (NICE) technology appraisal guidance Statins for the prevention of cardiovascular events.

Ethnicity, body mass index, and family history of premature heart disease should be routinely recorded in medical records.

The estimated CVD risk should be increased by a factor of 1.5 in people with a first-degree relative with a history of premature CHD (age at onset younger than

55 in fathers, sons or brothers or younger than 65 in mothers, daughters or sisters).

The estimated CVD risk should be increased by a factor of between 1.5 and 2.0 if more than one first-degree relative has a history of premature CHD.

The estimated CVD risk for men with a South Asian background should be increased by a factor of 1.4.

Socioeconomic status should be considered when using CVD risk scores to inform treatment decisions.

Severe obesity (body mass index greater than 40 kg/m^2) affects CVD risk and should be considered when using risk scores to inform treatment decisions (see the NGC summary of the NICE clinical guideline Obesity.

CVD risk may be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking. Clinical judgement should be used to decide on further treatment of risk factors in people who are below the 20% CVD risk threshold.

CVD risk scores may not be appropriate as a way of assessing risk in people who are at increased CVD risk because of underlying medical conditions or treatments. These include people treated for human immunodeficiency virus (HIV) or with antipsychotic medication, people with chronic kidney disease (seeÂ the NGC summary of the NICE clinical guideline Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care) and people with autoimmune disorders such as systemic lupus erythematosus (SLE) and rheumatoid arthritis.

People aged 75 or older should be considered at increased risk of CVD, particularly people who smoke or have raised blood pressure. They are likely to benefit from statin treatment. Assessment and treatment should be guided by the benefits and risks of treatment, informed preference and comorbidities that may make treatment inappropriate.

Lipid Measurement

Both total and high density lipoprotein (HDL) cholesterol should be measured to achieve the best estimate of CVD risk with Framingham 1991 risk equations.

Before starting lipid modification therapy for primary prevention, people should have at least one fasting lipid sample taken to measure total cholesterol, low density lipoprotein (LDL) cholesterol, HDL cholesterol and triglycerides.

People in whom familial hypercholesterolaemia or other monogenic disorders are suspected because of a combination of clinical findings, lipid profiles and family history of premature CHD should be considered for further investigation and specialist review.

People with severe hyperlipidaemia should be considered for further investigation and/or specialist review.

Communication about Risk Assessment and Treatment

Healthcare professionals should use every day, jargon-free language to communicate information on risk. If technical terms are used, these should be clearly explained.

Adequate time should be set aside during the consultation to provide information on risk assessment and to allow any questions to be answered. Further consultation may be required.

The discussion relating to the consultation on risk assessment and the person's decision should be documented.

People should be offered information about their absolute risk of CVD and about the absolute benefits and harms of an intervention over a 10-year period. This information should be in a form that:

- Presents individualised risk and benefit scenarios
- Presents the absolute risk of events numerically
- Uses appropriate diagrams and text

(See www.npci.org.uk)

In order to encourage the person to participate in reducing their CVD risk, the healthcare professional should:

- Find out what, if anything, the person has already been told about their CVD risk and how they feel about it
- Explore the person's beliefs about what determines future health (this may affect their attitude to changing risk)
- Assess their readiness to make changes to their lifestyle (diet, physical activity, smoking and alcohol consumption), to undergo investigations and to take medication
- Assess their confidence in making changes to their lifestyle, undergoing investigations and taking medication
- Inform them of potential future management based on current evidence and best practice
- Involve them in developing a shared management plan
- Check with them that they have understood what has been discussed

People should be informed that CVD risk equations can only provide an estimate of risk. However, the likelihood of misclassification is reduced as the estimated CVD risk increases above the threshold of 20% risk over 10 years.

If the person's CVD risk is considered to be at a level that merits intervention but they decline the offer of treatment, they should be advised that their CVD risk should be considered again in the future.

Lifestyle Modifications for the Primary and Secondary Prevention of CVD

Cardioprotective Diet

People at high risk of or with CVD should be advised to eat a diet in which total fat intake is 30% or less of total energy intake, saturated fats are 10% or less of total energy intake, intake of dietary cholesterol is less than 300 mg/day and where possible saturated fats are replaced by monounsaturated and polyunsaturated fats. It may be helpful to suggest they look at www.eatwell.gov.uk/healthydiet for further practical advice.

People at high risk of or with CVD should be advised to eat at least five portions of fruit and vegetables per day, in line with national guidance for the general population. Examples of what constitutes a portion can be found at www.eatwell.gov.uk/healthydiet and www.5aday.nhs.uk.

People at high risk of or with CVD should be advised to consume at least two portions of fish per week, including a portion of oily fish. Further information and advice on healthy cooking methods can be found at www.eatwell.gov.uk/healthydiet.

Pregnant women should be advised to limit their oily fish to no more than two portions per week. Further information and advice on oily fish consumption can be found at www.eatwell.gov.uk/healthydiet.

People should not routinely be recommended to take omega-3 fatty acid supplements for the primary prevention of CVD.

Plant Stanols and Sterols

People should not routinely be recommended to take plant sterols and stanols for the primary prevention of CVD.

Physical Activity

People at high risk of or with CVD should be advised to take 30 minutes of physical activity a day, of at least moderate intensity, at least 5 days a week, in line with national guidance for the general population (Department of Health [2004]. At least five a week: evidence on the impact of physical activity and its relationship to health. A report from the Chief Medical Officer. London: Department of Health. Available from www.dh.gov.uk).

People who are unable to perform moderate-intensity physical activity at least 5 days a week because of comorbidity, medical conditions or personal circumstances should be encouraged to exercise at their maximum safe capacity.

Recommended types of physical activity include those that can be incorporated into everyday life, such as brisk walking, using stairs and cycling (see 'At least five a week') (Department of Health [2004]. At least five a week: evidence on the impact of physical activity and its relationship to health. A report from the Chief Medical Officer. London: Department of Health. Available from www.dh.gov.uk).

People should be advised that bouts of physical activity of 10 minutes or more accumulated throughout the day are as effective as longer sessions (see 'At least five a week') (Department of Health [2004]. At least five a week: evidence on the impact of physical activity and its relationship to health. A report from the Chief Medical Officer. London: Department of Health. Available from www.dh.gov.uk).

Advice about physical activity should take into account the person's needs, preferences and circumstances. Goals should be agreed and the person should be provided with written information about the benefits of activity and local opportunities to be active, in line with the NGC summary of the NICE public health intervention guidance Physical activity.

Combined Interventions (Diet and Physical Activity)

Advice on diet and physical activity should be given in line with national recommendations (see www.eatwell.gov.uk/healthydiet).

Weight Management

People at high risk of or with CVD who are overweight or obese should be offered appropriate advice and support to work towards achieving and maintaining a healthy weight, in line with the NGC summary of theÂ NICE clinical guideline Obesity.

Alcohol Consumption

Alcohol consumption for men should be limited to up to 3-4 units a day. For women, alcohol consumption should be limited to up to 2–3 units a day. People should avoid binge drinking. Further information can be found at www.eatwell.gov.uk/healthydiet.

Smoking Cessation

All people who smoke should be advised to stop, in line with the NGC summary of the NICEÂ public health guidance Smoking cessation services.

People who want to stop smoking should be offered support and advice, and referral to an intensive support service (for example, the National Health Service [NHS] Stop Smoking Services).

If a person is unable or unwilling to accept a referral to an intensive support service they should be offered pharmacotherapy in line with the NGC summary of the NICE public health guidance on Smoking cessation services and see the NGC summary of the NICE technology appraisal guidance Varenicline for smoking cessation.

Drug Therapy for the Primary and Secondary Prevention of CVD

When considering lipid modification therapy in primary and secondary prevention, drugs are preferred for which there is evidence in clinical trials of a beneficial effect on CVD morbidity and mortality.

Drug Therapy for Primary Prevention

Before offering lipid modification therapy for primary prevention, all other modifiable CVD risk factors should be considered and their management optimised if possible. Baseline blood tests and clinical assessment should be performed, and comorbidities and secondary causes of dyslipidaemia should be treated. Assessment should include:

- Smoking status
- Alcohol consumption
- Blood pressure (see Hypertension, NICE clinical guideline 34)
- Body mass index or other measure of obesity (see the NGC summary ofÂ the NICE clinical guideline Obesity)
- Fasting total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides (if fasting levels are not already available)
- Fasting blood glucose
- Renal function
- Liver function (transaminases)
- Thyroid-stimulating hormone (TSH) if dyslipidaemia is present

Statins for Primary Prevention

Statin therapy is recommended as part of the management strategy for the primary prevention of CVD for adults who have a 20% or greater 10-year risk of developing CVD. This level of risk should be estimated using an appropriate risk calculator, or by clinical assessment for people for whom an appropriate risk calculator is not available or appropriate (for example, older people, people with diabetes or people in high-risk ethnic groups). (Note: This recommendation has been taken fromÂ the NGC summary of the NICE technology appraisal guidance Statins for the prevention of cardiovascular events).

The decision whether to initiate statin therapy should be made after an informed discussion between the responsible clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as comorbidities and life expectancy. (Note: This recommendation has been taken from the NGC summary of the NICE technology appraisal guidance Statins for the prevention of cardiovascular events).

If statin treatment is appropriate, it should be offered as soon as practicable after a full risk factor assessment.

When the decision has been made to prescribe a statin, it is recommended that therapy should usually be initiated with a drug with a low acquisition cost (taking into account required daily dose and product price per dose). (Note: This recommendation has been taken from the NGC summary of the NICE technology appraisal guidance Statins for the prevention of cardiovascular events).

Treatment for the primary prevention of CVD should be initiated with simvastatin 40 mg. If there are potential drug interactions, or simvastatin 40 mg is contraindicated, a lower dose or alternative preparation such as pravastatin may be chosen.

Higher intensity statins should not routinely be offered to people for the primary prevention of CVD. (Note: 'Higher intensity statins' are statins used in doses that produce greater cholesterol lowering than simvastatin 40 mg, for example simvastatin 80 mg.)

A target for total or LDL cholesterol is not recommended for people who are treated with a statin for primary prevention of CVD.

Once a person has been started on a statin for primary prevention, repeat lipid measurement is unnecessary. Clinical judgement and patient preference should guide the review of drug therapy and whether to review the lipid profile.

Fibrates for Primary Prevention

Fibrates should not routinely be offered for the primary prevention of CVD. If statins are not tolerated, fibrates may be considered.

Nicotinic Acid for Primary Prevention

Nicotinic acid should not be offered for the primary prevention of CVD.

Anion Exchange Resins for Primary Prevention

Anion exchange resins should not routinely be offered for the primary prevention of CVD. If statins are not tolerated, an anion exchange resin may be considered.

Ezetimibe for Primary Prevention

People with primary hypercholesterolaemia should be considered for ezetimibe treatment in line with the NGC summary of theÂ NICE technology appraisal guidance Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia.

Combination Therapy for Primary Prevention

The combination of an anion exchange resin, fibrate or nicotinic acid with a statin should not be offered for the primary prevention of CVD.

The combination of a fish oil supplement with a statin should not be offered for the primary prevention of CVD.

Drug Therapy for Secondary Prevention

For secondary prevention, lipid modification therapy should be offered and should not be delayed by management of modifiable risk factors. Blood tests and clinical assessment should be performed, and comorbidities and secondary causes of dyslipidaemia should be treated. Assessment should include:

- Smoking status
- Alcohol consumption

- Blood pressure (see Hypertension, NICE clinical guideline 34)
- Body mass index or other measure of obesity (see the NGC summary of the NICE clinical guideline Obesity)
- Fasting total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides (if fasting levels are not already available)
- Fasting blood glucose
- Renal function
- Liver function (transaminases)
- Thyroid-stimulating hormone (TSH) if dyslipidaemia is present

If a person has acute coronary syndrome, statin treatment should not be delayed until lipid levels are available. A fasting lipid sample should be taken about 3 months after the start of treatment.

Statins for Secondary Prevention

Statin therapy is recommended for adults with clinical evidence of CVD.Â (Note: This recommendation has been taken from the NGC summary of the NICEÂ technology appraisalÂ guidance Statins for the prevention of cardiovascular events).

The decision whether to initiate statin therapy should be made after an informed discussion between the responsible clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as comorbidities and life expectancy.Â (Note: This recommendation has been taken from the NGC summary of the NICEÂ technology appraisal guidance Statins for the prevention of cardiovascular events).

When the decision has been made to prescribe a statin, it is recommended that therapy should usually be initiated with a drug with a low acquisition cost (taking into account required daily dose and product price per dose).Â (Note: This recommendation has been taken from the NGC summary of the NICEÂ technology appraisal guidance Statins for the prevention of cardiovascular events).

People with acute coronary syndrome should be treated with a higher intensity statin. Any decision to offer a higher intensity statin should take into account the patient's informed preference, comorbidities, multiple drug therapy, and the benefits and risks of treatment.Â (Note: 'Higher intensity statins' are statins used in doses that produce greater cholesterol lowering than simvastatin 40 mg, for example simvastatin 80 mg.)

Treatment for the secondary prevention of CVD should be initiated with simvastatin 40 mg. If there are potential drug interactions, or simvastatin 40 mg is contraindicated, a lower dose or alternative preparation such as pravastatin may be chosen.

In people taking statins for secondary prevention, consider increasing to simvastatin 80 mg or a drug of similar efficacy and acquisition cost if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained. Any decision to offer a higher intensity statin should take into account informed preference, comorbidities, multiple drug therapy, and the benefit and risks of treatment. (Note: 'Higher intensity statins' are statins

used in doses that produce greater cholesterol lowering than simvastatin 40 mg, for example simvastatin 80 mg.)

An 'audit' level of total cholesterol of 5 mmol/litre should be used to assess progress in populations or groups of people with CVD, in recognition that more than a half of patients will not achieve a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre.

Fibrates for Secondary Prevention

Fibrates may be considered for secondary prevention in people with CVD who are not able to tolerate statins.

Nicotinic Acid for Secondary Prevention

Nicotinic acid may be considered for secondary prevention in people with CVD who are not able to tolerate statins.

Anion Exchange Resins for Secondary Prevention

Anion exchange resins may be considered for secondary prevention in people with CVD who are not able to tolerate statins.

Ezetimibe for Secondary Prevention

People with primary hypercholesterolaemia should be considered for ezetimibe treatment in line with the NGC summary of the NICEÂ technology appraisal guidance Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia.

Monitoring of Statin Treatment for Primary and Secondary Prevention

If a person taking a statin starts taking additional drugs, or needs treatment for a concomitant illness that interferes with metabolic pathways or increases the propensity for drug and food interactions, consider reducing the dose of the statin, or temporarily or permanently stopping it.

People who are being treated with a statin should be advised to seek medical advice if they develop muscle symptoms (pain, tenderness or weakness). If this occurs, creatine kinase should be measured.

Creatine kinase should not be routinely monitored in asymptomatic people who are being treated with a statin.

Baseline liver enzymes should be measured before starting a statin. Liver function (transaminases) should be measured within 3 months of starting treatment and at 12 months, but not again unless clinically indicated.

People who have liver enzymes (transaminases) that are raised but are less than 3 times the upper limit of normal should not be routinely excluded from statin therapy.

If a person develops an unexplained peripheral neuropathy, statins should be discontinued and specialist advice sought.

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the full version of the original guideline document (seeÂ the "Availability of Companion Documents" field):

- Primary prevention care pathway
- Secondary prevention care pathway

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate cardiovascular risk assessment and primary and secondary prevention of cardiovascular disease (CVD)

POTENTIAL HARMS

Statin therapy has been associated with the following adverse events: myalgia, myopathy, asthenia, creatine kinase elevation, elevated liver function tests, and rhabdomyolysis.

Refer to the full version of the guideline for a detailed discussion of adverse effects related to statins and other drug therapy used in primary and secondary prevention.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of

their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' (available from www.dh.gov.uk). Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (listed below). These are available on NICE web site (http://guidance.nice.org.uk/CG67) (see also the "Availability of Companion Documents" field):

- Slides highlighting key messages for local discussion
- Costing tools:
    - Costing report to estimate the national savings and costs associated with implementation
    - Costing template to estimate the local costs and savings involved
- Audit support for monitoring local practice

Key Priorities for Implementation

Primary Prevention of Cardiovascular Disease (CVD)

- For the primary prevention of CVD in primary care, a systematic strategy should be used to identify people aged 40–74 who are likely to be at high risk.
- People should be prioritised on the basis of an estimate of their CVD risk before a full formal risk assessment. Their CVD risk should be estimated using CVD risk factors already recorded in primary care electronic medical records.
- The Framingham 1991 10-year risk equations should be used to assess CVD risk. CVD risk should be calculated as:

  CVD risk = 10-year risk of fatal and non-fatal stroke, including transient ischaemic attack + 10-year risk of coronary heart disease (CHD)[a]

  [a] CHD risk includes the risks of death from CHD, and non-fatal CHD, including silent myocardial infarction, angina and coronary insufficiency (acute coronary syndrome).

- People should be offered information about their absolute risk of CVD and about the absolute benefits and harms of an intervention over a 10-year period. This information should be in a form that:
    - Presents individualised risk and benefit scenarios

    - Presents the absolute risk of events numerically
    - Uses appropriate diagrams and text

  (See www.npci.org.uk)

- Before offering lipid modification therapy for primary prevention, all other modifiable CVD risk factors should be considered and their management optimised if possible. Baseline blood tests and clinical assessment should be performed, and comorbidities and secondary causes of dyslipidaemia should be treated. Assessment should include:
    - Smoking status
    - Alcohol consumption
    - Blood pressure (see Hypertension, NICE clinical guideline 34)
    - Body mass index or other measure of obesity (see the NGC summary of the NICE the clinical guideline Obesity)
    - Fasting total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides (if fasting levels are not already available)
    - Fasting blood glucose
    - Renal function
    - Liver function (transaminases)
    - Thyroid-stimulating hormone (TSH) if dyslipidaemia is present
- Statin therapy is recommended as part of the management strategy for the primary prevention of CVD for adults who have a 20% or greater 10-year risk of developing CVD. This level of risk should be estimated using an appropriate risk calculator, or by clinical assessment for people for whom an appropriate risk calculator is not available or appropriate (for example, older people, people with diabetes or people in high-risk ethnic groups).
- Treatment for the primary prevention of CVD should be initiated with simvastatin 40 mg. If there are potential drug interactions, or simvastatin 40 mg is contraindicated, a lower dose or alternative preparation such as pravastatin may be chosen.

Secondary Prevention of CVD

- For secondary prevention, lipid modification therapy should be offered and should not be delayed by management of modifiable risk factors. Blood tests and clinical assessment should be performed, and comorbidities and secondary causes of dyslipidaemia should be treated. Assessment should include:
    - Smoking status
    - Alcohol consumption
    - Blood pressure (see Hypertension, NICE clinical guideline 34)
    - Body mass index or other measure of obesity (see the NGC summary of the NICE the clinical guideline Obesity)
    - Fasting total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides (if fasting levels are not already available)
    - Fasting blood glucose
    - Renal function
    - Liver function (transaminases)
    - Thyroid-stimulating hormone (TSH) if dyslipidaemia is present
- Statin therapy is recommended for adults with clinical evidence of CVD.

- People with acute coronary syndrome should be treated with a higher intensity statin. Any decision to offer a higher intensity statin should take into account the patient's informed preference, comorbidities, multiple drug therapy, and the benefits and risks of treatment.
- Treatment for the secondary prevention of CVD should be initiated with simvastatin 40 mg. If there are potential drug interactions, or simvastatin 40 mg is contraindicated, a lower dose or alternative preparation such as pravastatin may be chosen.
- In people taking statins for secondary prevention, consider increasing to simvastatin 80 mg or a drug of similar efficacy and acquisition cost if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained. Any decision to offer a higher intensity statin should take into account informed preference, comorbidities, multiple drug therapy, and the benefit and risks of treatment.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Primary Care. Lipid modification. Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 37 p. (Clinical guideline; no. 67).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 May

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Primary Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At each Guideline Development Group (GDG) meeting, all GDG members declared any potential conflict of interests. Declarations are listed in Appendix L of the full version of the original guideline document (see "Availability of Companion Documents" field).

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Lipid modification. Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 239 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Lipid modification. Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2008 May. 16 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Lipid modification. Costing report. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2008 May. 43 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Lipid modification. Costing template. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2008. Various p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Lipid modification. Implementing NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence; 2008. 16 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Lipid modification. Audit support. London (UK): National Institute for Health and Clinical Excellence; 2008. 11 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 April. Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0845 003 7783. ref: N1574. 11 Strand, London, WC2N 5HR.

Additional accompanying guideline materials can be found from the National Institute for Health and Clinical Excellence (NICE) Web site.

PATIENT RESOURCES

The following is available:

- Lowering cholesterol to reduce the risk of heart disease, stroke and peripheral arterial disease. Understanding NICE guidance -Â Information for people who use NHS services. London (UK): National Institute for Health and Clinical

Excellence; 2008 May. 12 p. (Clinical guideline; no. 67). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response LineÂ 0845 003 7783. ref: N1575. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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